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10/505,213	11/22/2004	Suzanne Margaret Price	114.1007	5907

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EXAMINER	
MYERS, CARLA J	
ART UNIT	PAPER NUMBER
1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,213	PRICE, SUZANNE MARGARET	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9,12,13 and 15-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-9, 12, 13, and 15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 7, 2008 has been entered.

2. Applicants' arguments and amendments to the claims have been fully considered but are not persuasive to place each of the claims in condition for allowance. All rejections not reiterated herein are hereby withdrawn. In particular, the rejection of claims 3, 4 and 14 under 35 U.S.C. 112, second paragraph, has been obviated by the amendments to the claims.

3. Claims 1-2, 4-9, 12, 13, and 15-19 are pending and have been examined herein. It is noted that claim 8 has been examined only to the extent that the claim reads on the elected invention of methods wherein the pretreatment is an enzymatic pretreatment.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite over the recitation of "wherein the method of pretreating a nucleic acid is PCR…" because it is not clear as to how this recitation is intended to further limit the claim. Claim 12 as written is inclusive of a method that requires only a step of performing PCR, mitochondrial DNA sequence, single nucleotide polymorphism analysis or low copy number PCR. However, claim 1 recites that the method of pretreating requires a step of pretreating to remove or inactivate contaminating nucleic acids. Claim 12 does not clarify how only the step of PCR accomplishes the objective of removing or inactivating contaminating nucleic acids. Thereby, it is unclear as to whether claim 12 is intended to be limited to, for example, a method which further comprises performing PCR, mitochondrial DNA sequence, etc, or if claim 12 is intended to be limited to a method wherein following the pretreating step, the sample can be analyzed by PCR, etc.

Maintained Rejections

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-9 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Walker (EP 0585660; cited in the IDS).

This rejection was previously presented in the Office action of January 4, 2008 and has been modified herein to address the amendments to the claims.

Walker teaches a method for analyzing a nucleic acid sample obtained from a site wherein the method comprises: i) pretreating the nucleic acid sample with a single-strand specific exonuclease to remove or inactivate contaminating nucleic acids obtained from the site; and ii) amplifying the pretreated sample to thereby analyze the nucleic acid sample (see, e.g., page 2, lines 24-34 and page 4, lines 43-46). In the method of Walker, the step of treating the nucleic acid sample with a single-strand specific exonuclease constitutes a step of pretreating the sample.

Regarding the recitation that the contaminating nucleic acids were purposefully added to the sample, Walker teaches that 1000 amplicons (i.e., contaminating nucleic acids) were added to the sample. The addition of the 1000 amplicons would serve to confound future analysis of target nucleic acids present in the sample. Further, it is noted that the recitation of why the contaminating nucleic acids are present in the sample (i.e., for the intention of confounding future analysis of target nucleic acids) is a mental step and thereby is not considered to materially limit the claims, or distinguish the claims over the method of Walker.

Additionally, in the method of Walker, the sample is contaminated with laboratory derived nucleic acids. This type of nucleic acid meets the limitations of the claims since such a nucleic has been introduced into the sample in the laboratory and confounds

future analysis of the sample. Again, the intention behind why the nucleic acid is present in the sample is a mental concept and does not materially limit the claims. The claims do not recite an active process step of adding a contaminating nucleic acid to a sample and/or do not recite any additional active process steps which distinguish the claims over the method of Walker. The method of Walker includes each of the active process steps of the present claims, and thereby anticipates the present claims, since Walker also teaches a method comprising pretreating a sample prior to analysis to remove or inactivate contaminating laboratory nucleic acids present in the sample which confound future analysis of target nucleic acids present in the sample.

Regarding claim 2, in the method of Walker, the nucleic acid is DNA (see, e.g., page 4, lines 3-15 and Example 2).

Regarding claim 4, Walker teaches that the contaminating nucleic acid may be an amplicon from a previous PCR (see, e.g. page 2, lines 7-13).

Regarding claim 5, the contaminating nucleic acid is considered to be degradation resistant since DNA is substantially more stable than other molecules and is resistant to many enzymes, such as RNases.

Regarding claim 6, the contaminating nucleic acid is considered to be synthetic since nucleic acids that have been synthesized by some process such as an amplification process constitute synthetic nucleic acids.

Regarding claim 7, the method of Walker is one in which the pretreatment preferentially removes or inactivates nucleic acids produced by other amplification

processes and thereby removes or inactivates nucleic acids that are free or substantially free of other cell components.

Regarding claims 8 and 9, the pretreatment step of Walker comprises treating the nucleic acid sample using an exonuclease (page 2, lines 24-30).

Regarding claim 12, Walker (page 2, lines 40-53) teaches that following the pretreatment step, the nucleic acid sample may be analyzed by any amplification method, including the method of PCR.

Response to Remarks:

In the response, Applicant's traversed this rejection by stating that "Walker fails to disclose removal of nucleic acids which are purposefully introduced into the sample as contaminants *prior to the analysis of the sample*." This argument has been fully considered but is not persuasive. In the method of Walker, the sample to be analyzed is first modified to include "1000 added amplicons" (page 5, lines 54-56). Thereby, Walker does in fact teach a method which removes contaminating nucleic acids (i.e., amplicons) that were purposefully added to the sample. The presence of the 1000 amplicons serves to confound future analysis of target nucleic acids present in the sample. Further, the amplicons are introduced prior to analysis (i.e., prior to performing PCR to detect the presence of target nucleic acids).

Additionally, Walker teaches a method in which laboratory derived contaminating nucleic acids are removed from a sample. Applicants assert that such nucleic acids are products of an amplification reaction and therefore are introduced during analysis and not prior to analysis. This argument has also been fully considered but is not

persuasive. The laboratory derived nucleic acids are introduced into the sample prior to analysis of that sample for the presence of a target nucleic acid. While other methods of analysis may have occurred in the same laboratory in order to produce the contaminating amplicons, the claims do not exclude such an occurrence. There is no requirement in the claims that the laboratory has never before performed a method of analysis. Rather, the claims require only a step of "pretreating the sample prior to analysis." In the method of Walker, the samples are pretreated prior to analysis because the samples are pretreated with exonuclease prior to performing the PCR analysis to detect the presence of the target nucleic acid.

Applicants assert that "Amplicons are products of a nucleic acid amplification reaction, and are therefore introduced during analysis of the sample – not contaminants which are purposefully introduced to confound future analysis of the sample." This argument has also been fully considered but is not persuasive because the present claims do in fact encompass methods in which the contaminating nucleic acid is an amplicon - see claim 4 which recites "wherein the contaminating nucleic acid is an amplicon derived from a PCR or another DNA amplification process."

The response states that Walker does not teach that the contaminating nucleic acids are "introduced prior to any analysis" conducted on the sample. this argument is not convincing because it is directed to limitations that are not recited in the claims. The claims require only that pretreatment occurs prior to analysis. The claims do not require introducing a contaminating nucleic acid prior to any analysis of the sample. Even if this limitation was recited in the claims, the method of Walker would still anticipate the

claimed invention since Walker teaches that 1000 amplicons (contaminating nucleic acids) are added to a sample prior to analyzing that sample by PCR. Walker also teaches a method wherein the contaminating amplicons are introduced into the sample in the laboratory and thereby are present in the sample prior to the analysis of that sample by PCR to detect target nucleic acids in the sample.

The response further states that the method of Walker would be unable to determine the presence of contamination in samples contaminated prior to their analysis in the laboratory. This argument is also not convincing because it is directed to limitations that are not recited in the claims. The claims do not require detecting contamination, nor do the claims require that contamination occurs prior to any type of analysis in a laboratory.

6. Claims 1-2, 5, 6, 7, 8, 9, 12, 13 and 15-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Miwa (U.S. Patent No. 4,514,502).

Miwa teaches a method for analyzing a nucleic acid sample obtained from a site wherein the method comprises: i) pretreating the nucleic acid sample with a RNase to remove or inactivate contaminating nucleic acids obtained from the site; and ii) analyzing the pretreated nucleic acid sample (see, e.g., col. 6, lines 56-68 through col. 7, lines 1-6 and 48-51). In the method of Miwa, the step of treating the nucleic acid sample with RNase constitutes a step of pretreating the sample to remove or inactivate contaminating RNA.

Regarding the recitation that the contaminating nucleic acid is purposefully introduced to the sample to confound future analysis of target nucleic acids in the

sample, in the method of Miwa, the contaminating RNA is present in the sample prior to analysis of the nucleic acids in the sample by gel electrophoresis. It is a property of the RNA that its presence would confound future analysis of target nucleic acids present in a sample. Further, it is noted that the recitation of why the contaminating nucleic acids are present in the sample (i.e., for the intention of confounding future analysis of target nucleic acids) is a mental step and thereby is not considered to materially limit the claims, or distinguish the claims over the method of Miwa. The claims do not recite an active process step of adding a contaminating nucleic acid to a sample and/or do not recite any additional active process steps which distinguish the claims over the method of Miwa. The method of Miwa includes each of the active process steps of the present claims, and thereby anticipates the present claims, since Miwa also teaches a method comprising pretreating a sample prior to analysis to remove or inactivate contaminating RNA present in the sample which confound future analysis of target nucleic acids present in the sample.

Regarding claim 2, in the method of Miwa, the contaminating nucleic acid present in the sample is RNA (see, e.g., col. 6, lines 56-68 through col. 7, lines 1-6).

Regarding claim 5, the contaminating nucleic acid is considered to be degradation resistant since RNA is resistant to many enzymes, such as DNases.

Regarding claim 6, the contaminating nucleic acid is considered to be synthetic since RNA present in a bacterial cell has been synthesized.

Regarding claim 7, pretreatment with RNase occurs after lysis of the cells and centrifugation to remove cellular components (col. 6, line 56 through col. 7, line 3)..

Thereby, the pretreatment comprises treating the sample with RNase to remove nucleic acids (RNA) that are substantially free from other cell components.

Regarding claims 8 and 9, the pretreatment step of Miwa comprises treating the nucleic acid sample using the enzyme RNase (col. 6, lines 68-col. 7., line 1).

Regarding claim 12, it is a property of the resulting nucleic acid that it can be analyzed by PCR. Further, it is noted that claim 12 does not in fact require performing an active process step of PCR.

Regarding claims 13 and 15-19, Miwa (col. 6, lines 56-68) teaches that the bacterial cell is first lysed prior to treatment with RNase. Accordingly, the pretreatment steps of Miwa include removing cell bound nucleic acids from a cell by exposing the nucleic acids in the cells using a lysing procedure and then removing the nucleic acids using an RNase pretreatment step.

Regarding claim 15, the contaminating RNA is of bacterial origin since it is present in a bacterial cell.

Regarding claim 16, the bacterial cell has been engineered to carry a multicopy plasmid containing at least one amplicon (i.e., copies of DNA produced by natural amplification/replication of the plasmid; see col. 2, lines 22-25; col. 3, lines 3-50; col. 4, lines 38-45).

Response to Remarks:

In the response, Applicant's traversed this rejection by stating that Miwa is concerned only with removing laboratory-derived contamination of nucleic acids – contamination resulting during analysis, from the laboratory procedure itself. It is

asserted that Miwa does not teach removal of RNA introduced to prior to analysis of the sample.

This argument has been fully considered but is not persuasive. In the method of Miwa, the sample is contaminated with RNA (i.e., a nucleic acid introduced into the sample by lysis of bacterial cells) and the RNA confounds future analysis of target plasmid DNA in the sample. Accordingly, in the method of Miwa, the contaminating RNA meets the limitations in the present claims of a contaminating nucleic acid since the RNA is purposefully introduced into the sample and confounds future analysis of the sample. Further, the introduction of the RNA into the sample occurs prior to analysis of the sample by gel electrophoresis. Since the RNA is present in the sample prior to performing gel electrophoresis (i.e., the analysis step), the RNA was necessarily introduced into the sample prior to analysis.

Applicants state that Miwa teaches only contamination that occurs during laboratory analysis. This argument is not convincing because it is does not accurately describe the method of Miwa. Miwa does not teach that the RNA is added during the analysis step. Rather, Miwa teaches removing RNA present in a sample by RNase digestion prior to performing the analysis step of gel electrophoresis – i.e., "pretreating the sample prior to analysis" by PCR to remove RNA purposefully introduced to the sample.

New Grounds of Rejection

7. Claims 1, 2, 4-9, 12, 13 and 15-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Satishchandran et al (U.S. Patent No. 6,168,918).

Satishchandran teaches a method for analyzing a nucleic acid sample obtained from a site wherein the method comprises: i) pretreating the nucleic acid sample with DpnI restriction endonuclease to remove to remove or inactivate contaminating plasmid nucleic acids present in the sample; and ii) analyzing the pretreated nucleic acid sample (see, e.g., col. 5, lines 29-67; col. 7, lines 28-67). In the method of Satishchandran, the step of treating the nucleic acid sample with DpnI restriction endonuclease constitutes a step of pretreating the sample to remove or inactivate contaminating bacterial plasmid DNA.

Regarding the recitation that the contaminating nucleic acid is purposefully introduced to the sample to confound future analysis of target nucleic acids in the sample, in the method of Satishchandran, the contaminating plasmid DNA is purposefully introduced into eukaryotic cells prior to the analysis of the cells. It is a property of the plasmid DNA that its presence would confound future analysis of target chromosomal nucleic acids present in a sample. Further, it is noted that the recitation of why the contaminating nucleic acids are present in the sample (i.e., for the intention of confounding future analysis of target nucleic acids) is a mental step and thereby is not considered to materially limit the claims, or distinguish the claims over the method of Satishchandran. The claims do not recite an active process step of adding a contaminating nucleic acid to a sample and/or do not recite any additional active process steps which distinguish the claims over the method of Satishchandran. The method of Satishchandran includes each of the active process steps of the present claims, and thereby anticipates the present claims, since Satishchandran also teaches a

method comprising pretreating a sample prior to analysis to remove or inactivate contaminating plasmid DNA introduced into the sample which confounds future analysis of target chromosomal nucleic acids present in the sample.

Regarding claim 2, in the method of Satishchandran, the contaminating nucleic acid present in the sample is DNA (see, e.g., col. 7, lines 30-34).

Regarding claim 4, the contaminating plasmid DNA is a nucleic acid derived from "another DNA amplification process" since plasmid DNA is produced by replication in a cell (i.e., replication is considered to be a process of amplification since copies of plasmid DNA are produced).

Regarding claim 5, the contaminating plasmid DNA is considered to be degradation resistant since plasmid DNA is resistant to many enzymes, such as RNases.

Regarding claim 6, the contaminating nucleic acid is considered to be synthetic since plasmid DNA present in a cell has been synthesized.

Regarding claim 7, the pretreatment with DpnI occurs after lysis of the cells and isolation of nucleic acids to remove cellular components (e.g., col. 17, line 48 to col. 18, line 30). Thereby, the pretreatment comprises treating the sample with DpnI to remove nucleic acids (plasmid DNA) that are substantially free from other cell components.

Regarding claims 8 and 9, the pretreatment step of Satishchandran comprises treating the nucleic acid sample using the enzyme DpnI which is a restriction endonuclease (e.g., col. 1, lines 43-56; col. 4, lines 58-65).

Regarding claim 12, it is a property of the resulting nucleic acid that it can be analyzed by PCR. Further, Satishchandran teaches analysis of the pre-treated samples by PCR (col. 8, line 60 through col. 9, line 9).

Regarding claims 13-19, Satishchandran (e.g., col. 17, line 48 to col. 18, line 30; claims 12 and 18) teaches that the cell is first lysed prior to treatment with DpnI. Accordingly, the pretreatment steps of Satishchandran includes removing cell bound nucleic acids from a cell by exposing the nucleic acids in the cells using a lysing procedure and then removing or inactivating the contaminating plasmid DNA using a DpnI pretreatment step.

Regarding claim 15, the contaminating plasmid DNA is of bacterial origin since it is present in a bacterial cell (e.g., col. 14 lines 53-60).

Regarding claim 16, in the method of Satishchandran, the bacterial cell from which the plasmid is derived has been engineered to carry a multicopy plasmid containing at least one amplicon (i.e., copies of DNA produced by natural amplification/replication of the plasmid; see, e.g., col. 13, lines 3-5; col. 14 lines 53-60).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Carla Myers/
Primary Examiner, Art Unit 1634